REMARKS

Claims 23-29, 31-39, 68-80, 82 and 84-97 are pending in this application, with Claims 25, 26, 28, 35, 36, 69-71, 73-75, 77-79 and 85-94 withdrawn from consideration as being directed to a non-elected species, and with Claims 1-22, 30, 40-67, 81 and 83 canceled. A complete Listing of Claims with appropriate status identifier begins on page 2 of this communication.

By the present amendment, Claims 23, 33 and 76 have been amended without prejudice or disclaimer of any previously claimed subject matter. Support for the amendments can be found, inter alia, throughout the specification and the claims as originally filed. For example, support for the amendment to claims 23, 33, 76 can be found at e.g., page 12, lines 23-25. No new matter is introduced by the amendments provided herewith.

The amendment is made solely to promote prosecution without prejudice or disclaimer of any previously claimed subject matter. With respect to all amendments and cancelled claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover, have not acquiesced to any rejections or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Although claims 25, 26, 28, 35, 36, 69-71, 73-75, 77-79, and 85-94 have been withdrawn from consideration as being directed to a non-elected species, Applicants note that, upon allowance of a generic claim, Applicants will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 C.F.R. §1.141.

Applicants have carefully considered the points raised in the Office Action and believe that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance.

Provisional Rejections Under Judicially Created Doctrine of Obviousness-type Double Patenting

The instant claims stand provisionally rejected (Office Action, page 6, item 31) under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable

over claims 1-16 of co-pending U.S. Pat. Application No. 09/870,762 ("the '762 application"). Claims 33 and 82 stand provisionally rejected (Office Action, page 6, item 32) under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claim 6 of U.S. Pat. Application No. 10/851,574 ("the '574 application").

With regard to the provisional rejections, Applicants are willing to consider submitting a terminal disclaimer in the present application with regard to the '762 application and the '574 application should these applications issue as a patent prior to the present application. Accordingly, Applicants respectfully request that the current provisional rejections be deferred pending resolution in the '762 and '574 patent applications.

Rejections under 35 U.S.C. §112, first paragraph (enablement)

Claims 68, 72, 76, 84, and 97 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way so as to enable those skilled in the art to make and/or use the invention commensurate in scope with the claims. Office Action at page 7. In rejecting the claims, the Office asserts that the "instant specification lacks a concrete *in vivo* showing that a representative number of amylin agonist analogue or peptide species encompassed within the SEQ ID NO: 14 genus has obesity-relieving function in any human subject in need of the claimed method of treatment." *Id.* at page 12.

Applicants respectfully disagree with the Examiner's rejections under 35 U.S.C. § 112, first paragraph. However, solely in order to facilitate prosecution, Applicants have amended claim 76 without prejudice or disclaimer. As such, Applicants respectfully assert that the claim rejections are rendered moot.

The Office has not met the evidentiary burden to impose an enablement rejection. A specification that discloses how to use a claimed invention "must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein." *In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995), *quoting In re Marzocchi*, 439 F.2d 220, 223, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971) (emphasis in original). The Office has provided neither evidence supporting the rejection nor any explanation of why the specification allegedly fails to enable the claimed invention.

As such, it is submitted that Applicants have provided considerable direction and guidance, and have presented working examples such that it is well within the level of ordinary skill in the art to practice the invention without undue experimentation. The Office has not provided sufficient evidence to cast doubt on the guidance provided in the specification. Rather, the Office has provided generalizations regarding a lack of predictability in the art and the need for some experimentation.

Even assuming, *arguendo*, that the Office's generalization regarding the unpredictable state of the art is accepted, the conclusion that undue experimentation would be required to practice the claimed invention is inconsistent with the current state of the law. Specifically, the law provides that experimentation is not necessarily undue simply because it is complex, if the art typically engages in such experimentation. *See In re Certain Limited-Charge Cell Culture Microcarriers*, 221 U.S.P.Q. 1165, 1174, (Int'l Trade Comm'n 1983) *aff'd. sub nom., Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 U.S.P.Q. 428 (Fed. Cir. 1985).

In rejecting the claims, the Office impermissibly attempts to limit the invention to the scope of the examples. This is legally incorrect. As set forth in MPEP § 2164.02, "[f]or a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art (in view of level of skill, state of the art and the information in the specification) would expect the claimed genus could be used in that manner without undue experimentation." This is exactly what Applicants have provided. For example, Tables I - VIII and Examples 1-3 disclose data concerning methods for treating obesity by administering amylin or an amylin agonist to a human subject. Alone, this disclosure is sufficient such that one of ordinary skill in the art at the time the invention was made would have the ability to practice the invention commensurate in scope with the claims.

Applicants disagree with the Office's assertion that "[t]here is a lack of enablement of a representative number of amylin agonist analogue or peptide variant species within the SEQ ID NO: 14 genus, each having the required functional ability to obesity in a representative number of human subject species." *Id.* at page 10. Applicants respectfully submit that this is legally incorrect. There is no requirement to provide all of the ways that the claimed invention can be

practiced. MPEP § 2164.01(b). The enablement requirement is satisfied as long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim. Applicants have satisfied this requirement by disclosing that pramlintide, when administered to a human, has the ability to treat obesity. As amylin agonist analogue and peptide variant species within the SEQ ID NO: 14 genus are disclosed in the instant specification and well known in the art, one of ordinary skill in the art at the time the invention was made would have the ability to practice the methods of treating obesity without undue experimentation in a manner that is commensurate in scope with the claims. Specification, for example, at page 13, lines 1-22 and page 15, line 1 - page 19, line 15.

The enablement requirement is met if the description enables any mode of making and using the claimed invention. *Engel Indus., Inc. v. Lockformer Co.,* 946 F.2d 1528, 1533. At a minimum, Applicants have satisfied this requirement by characterizing methods of treating obesity by administering pramlintide to humans. Specification, for example, at Examples 1-3 and Tables I - VII. Moreover, Applicants have disclosed numerous amylin agonist analogue and peptide variant species within the SEQ ID NO: 14 genus that are capable of treating obesity. Specification, for example, at page 13, lines 1-22 and page 15, line 1 - page 19, line 15. Given at least this disclosure, one of ordinary skill in the art at the time the invention was made would have the ability to practice the claimed invention in a manner that is commensurate in scope with the claims without undue experimentation.

Applicants disagree with the Office's assertion that "[g]iven the breadth of the genus 'SEQ ID NO: 14', it is not possible to envisage what precise structure in the genus of 'SEQ ID NO: 14' provides for the required functionality, i.e., the ability to treat obesity in a generic human subject in need thereof." Office Action at page 9. Again, there is no requirement to provide all of the ways that the claimed invention can be practiced. MPEP § 2164.01(b). Moreover, one of ordinary skill in the art having read the specification would have the ability to test and select amylin agonist analogue and peptide variant species within the SEQ ID NO: 14 genus capable of treating obesity when administered to a human. For example, Example 7 in the instant specification provides for a method of evaluating compounds capable of binding to

amylin receptors. Given this, one skilled in the art would have the ability to test the amylin receptor binding efficacy and effectiveness of species within the SEQ ID NO: 14 genus, given at least the teachings of Example 7.

Applicants disagree with the Office's assertion that one of skill in the art would not be able to treat obesity by administering species within the SEQ ID NO: 14 genus to a human subject. *Id.* at page 16. The specification is replete with examples of functional variants, fragments, and derivatives of amylin and amylin agonists. Specification, for example, page 13, lines 1-22 and page 15, line 1 - page 19, line 15. For example, given the disclosure of SEQ ID NO:14, one of ordinary skill in the art having read the specification would have the ability to make amino acid substitutions to amylin agonist analogue and peptide variant species without undue experimentation. *Id.* Given this disclosure, one of ordinary skill in the art at the time the invention was made would also recognize which positions of the SEQ ID NO:14 genus are amenable to mutations and conservative substitutions. Moreover, to the extent that any additional experimentation may be required, Applicant notes that the performance of routine and well-known steps cannot create undue experimentation even if it is laborious. *See In re Wands*, 858 F.2d at 737, 8 U.S.P.Q.2d at 1404; *In re Angstadt,* 537 F.2d 498, 504, 190 U.S.P.Q. 214, 218-219 (C.C.P.A. 1976).

Given this disclosure, Applicants respectfully submit that one of ordinary skill in the art at the time the invention was made would have the ability to select variants, fragments, or amylin agonist analogue and peptide variant species within the SEQ ID NO: 14 genus for practice with the claimed methods without undue experimentation. Applicants have sufficiently described the claimed invention such that one of skill in the art in light of the specification would be able to practice the invention commensurate in scope with the claims. Taken in combination, such disclosure provides adequate direction, including working examples, to teach the skilled artisan how to make and use the claimed invention without undue experimentation.

Accordingly, for at least these reasons, it is submitted that the claims are sufficiently enabled under 35 U.S.C. § 112, first paragraph, and withdrawal of this rejection is respectfully requested.

Rejections under Judicially Created Doctrine of Obviousness-type Double Patenting

Claims 23, 24, 33 and 34

The rejection of Claims 23, 24, 33 and 34 (Office Action, page 12, item 34) under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 34 and 35 of U.S. Pat. No. 5,686,411 ("the '411 patent") as evidenced by Tsanev (Vutr. Boles 23:12-17, 1984, abstract), is respectfully traversed.

Claim 23 of the instant application as currently amended provides a method for treating obesity in a human subject in need of such treatment comprising administration of a composition containing a defined amount of an amylin or an amylin agonist, wherein the amount amylin or amylin agonist administered is effective to treat obesity in the subject, wherein the composition is not administered in conjunction with another obesity relief agent, and wherein the subject is in need of treatment for obesity. Claim 24, dependent on Claim 23, further requires that the amylin agonist is an amylin agonist analogue. Claim 33, as amended, provides a method for treating obesity in a human in need of treatment for obesity consisting of administering to a human subject an amount of a composition effective to treat obesity in the subject, the composition comprising a defined amount of an obesity relief agent consisting of an amylin or an amylin agonist and a pharmaceutically acceptable carrier.

In contrast, Claims 34 and 35 of the '411 patent are directed to methods for the treatment of diabetes mellitus in a mammal comprising the administration of a therapeutically effective amount of a particular amylin agonist analogue.

Furthermore, the cited claims of the '411 patent are silent with regard to treating obesity. Indeed, even if obesity is common among those with diabetes, a claim to treating diabetes mellitus with an amylin agonist analogue does not necessarily teach or suggest treating patients with obesity as claimed. Further, nothing in the cited claims teaches or suggests the use of an amylin or an amylin agonist in an amount effective to treat obesity. Yet further, nothing in the cited claims teaches or suggests the identification of a subject in need of treatment for obesity. Specifically, the courts have held that the phrase "in need thereof" (e.g., as recited in independent Claims 23, 33 and 76) is meaningful, and that "the claims' recitation of a patient or a human 'in need' gives life and meaning to the preambles' statement of purpose." Jansen v. Rexall

Sundown, Inc. 342 F.3d 1329, 1333 (Fed. Cir. 2003). Thus, since the cited claims do not teach or suggest treating obesity or the use of an amount effective to treat obesity, a skilled artisan would have no expectation of success for the claimed invention in view of the cited claims.

In an attempt to cure the deficiency in Claims 34 and 35 of the '411 patent, the Examiner relies on Tsanev to provide alleged evidence that 80-90% of diabetic patients are obese. The Examiner further asserts (Office action, page 13, lines 3-5) that "the method of the '411 patent comprising the administration of 0.1 to 5 mg, 0.5 to 1.0 mg or the amylin agonist 25,28,29Pro-human amylin to a diabetic patient anticipates the instant claims (emphasis added)."

Applicants disagree with the Examiner's assertion of inherent anticipation. Anticipation based on inherency is appropriate only when the prior art relied upon necessarily includes all of the elements of the claims in question, Atofina v. Great Lakes Chemical Corp., 441 F.3d 991, 78 USPQ2d 1417, 1424 (Fed. Cir. 2006), and is the natural result of following the instructions or examples of the prior art. SmithKline Beecham Corp. v. Apotex Corp., 403 F.3d 1331, 1334, 74 USPQ2d 1398, 1407 (Fed. Cir. 2005) (citing Schering Corp. v. Geneva Pharms., Inc., 339 F. 3d 1373, 1377, 67 USPQ2d 1664, 1667 (Fed. Cir. 2003)). The Court in Schering relied in part on the decision In re Cruciferous Sprouts Litigation, 301 F.3d 1343, 1351, 64 USPQ2d 1202, 1206 (Fed. Cir. 2002) wherein it was noted that to demonstrate inherency, it was necessary to show that the prior art necessarily, always functions in accordance with the claims addressed. The requirement that the teaching of a reference always, under any circumstances, necessarily satisfies the recitation of the claims to make out a case of inherent anticipation was reaffirmed by the Federal Circuit in Abbott Laboratories v. Baxter Pharmaceutical Products, Inc., 471 F.3d 1363, 1368 (Fed. Cir. 2006). It is well settled that a determination of inherency cannot be established by probabilities or possibilities, but that it is incumbent upon the Examiner to establish the inevitability of the inherency which is propounded. In re Oelrich, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981); In re Wilding, 535 F.2d 631, 635-36, 190 USPQ 59, 63-64 (CCPA 1976).

As acknowledged by the Examiner (Office Action, page 13, line 1), Tsanev discloses that 80-90% of diabetic patients are obese. Accordingly, 80-90% falls short of the 100% (i.e., always, under any circumstanes) criterion required by the claims and required by the law. Accordingly,

Claims 34 and 35 of the '411 patent do not support prima facie obviousness with regard to the claimed invention, and Applicants respectfully request reconsideration and withdrawal of the present rejection.

Claims 23 and 33

The rejection of Claims 23 and 33 Office Action, page 13, item 35) under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over Claims 11 and 13 of U.S. Pat. No. 5,321,008 (hereinafter "the '008 patent) as evidenced by Tsanev and by U.S. Pat. No. 5,739,106 (hereinafter "the '106 patent"), is respectfully traversed.

The cited claims of the '008 patent are silent with regard to treating obesity. Even if obesity is common among those with diabetes, a claim to treating diabetes mellitus does not necessarily teach or suggest treating patients with obesity as claimed. Similar to the rejection based on the '411 patent above, the Examiner's attempts to cure the deficiencies of the '008 patent by citing the alleged prevalence of intrinic obesity (80-90% according to Tsanev) which falls short of the 100% required by the claims and required by the law. Furthermore, since the cited claims do not teach or suggest treating obesity or the use of an amount effective to treat obesity, a skilled artisan would have no expectation of success for the claimed invention in view of the cited claims. Thus, claims 11 and 13 of the '008 patent do not support prima facie obviousness with regard to the claimed invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of the present rejection.

Rejections under 35 U.S.C. §112, first paragraph (New Matter)

The rejection of Claims 23, 33 and 76 under 35 U.S.C. § 112, first paragraph (Office Action, page 14, item 36) as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, is respectfully traversed.

The argument set forth by the Examiner in the current rejection appears related to the term "composition" (e.g., at Office Action, page 15, lines 5, 8 and 11), which term appeared in then-new Claims 23 and 33 of the Response filed December 14, 2002, and in then-new Claim 76 of the Response filed February 24, 2006. As well understood by one of ordinary skill in the art,

compositions useful in the invention necessarily contain the amylin or amylin agonist contemplated in Claims 23, 33 and 76. Indeed, express support for the term "composition" contemplated for use in the methods of the invention is found in the specification as originally filed, at e.g., page 24, lines 16-19: "Compositions useful in the invention may conveniently be provided in the form of formulations suitable for parenteral (including intravenous, intramuscular and subcutaneous) or nasal or oral administration."

Accordingly, Applicants respectfully request reconsideration and withdrawal of the present rejection for alleged new matter. Furthermore, Applicants respectfully request that the priority of the instant application be accorded the filing date of the priority document.

Rejections under 35 U.S.C. §112, first paragraph (Scope of Enablement)

Claims 23, 24, 27, 29, 31-34, 37-39, 80, 82, 95 and 96 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way so as to enable those skilled in the art to make and/or use the invention commensurate in scope with the claims. Office Action at page 16. In rejecting the claims, the Office asserts that the specification "does not reasonably provide enablement for a method of treating obesity in any human subject including a non-type 2 or a non-type 1 diabetic human subject in need thereof, or a type 1 or type 2 diabetic human subject in need thereof who is not on insulin therapy, comprising administering any 'amylin', any 'amylin agonist', or any 'amylin agonist analogue' other than pramlintide by any route other than 'subcutaneous' route, and in any amount other than those identified above TID or QID." *Id.*

Applicants respectfully disagree with the Examiner's rejections under 35 U.S.C. § 112, first paragraph. However, solely in order to facilitate prosecution, Applicants have amended claims 23, 33 and 76 without prejudice or disclaimer. As such, Applicants respectfully assert that the claim rejections are rendered moot.

Applicants thank the Office for the acknowledgment that the specification is enabling for "for a method of reducing the body weight of an insulin-requiring type II diabetic human subject having a BMI of at least or less than 27 kg/m^2 comprising subcutaneous adjunctive administration to said subject, before each meal three times a day, 30, 75 or 150 micrograms TID of an amylin agonist which is ^{25,28,29}Pro-h-amylin, i.e., pramlintide, for 52 weeks, and a method

of reducing the body weight of an insulin-requiring human subject having type 1 diabetes mellitus having a BMI of at least 27 kg/m^2 comprising subcutaneous adjunctive administration to said subject, before each meal four times a day, 30 micrograms of pramlintide for 20 weeks followed by either 30 or 60 micrograms of pramlintide QID up to week 52, of an amylin agonist which is ^{25,28,29}Pro-h-amylin, i.e. pramlintide, wherein said pramlintide is not administered in conjunction with another obesity relief agent, wherein the body weight of said human subject is significantly reduced after 13, 26 and 52 weeks of said treatment compared to the body weight of the placebo group." *Id.* Indeed, the specification discloses numerous methods of treating obesity in a human comprising administering amylin or an amylin agonist to a human subject. Specification, for example, at Examples 1-3 and Tables I - VII. Given at least this, Applicants respectfully submit that the claimed invention could be practiced by one of ordinary skill in the art with no undue experimentation.

The Office has not met the evidentiary burden to impose an enablement rejection. A specification that discloses how to use a claimed invention "must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein." *In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995), *quoting In re Marzocchi*, 439 F.2d 220, 223, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971) (emphasis in original). The Office has provided neither evidence supporting the rejection nor any explanation of why the specification allegedly fails to enable the claimed invention.

As such, it is submitted that Applicants have provided considerable direction and guidance, and have presented working examples such that it is well within the level of ordinary skill in the art to practice the invention without undue experimentation. The Office has not provided sufficient evidence to cast doubt on the guidance provided in the specification. Rather, the Office has provided generalizations regarding a lack of predictability in the art and the need for some experimentation.

Even assuming, *arguendo*, that the Office's generalization regarding the unpredictable state of the art is accepted, the conclusion that undue experimentation would be required to practice the claimed invention is inconsistent with the current state of the law. Specifically, the

law provides that experimentation is not necessarily undue simply because it is complex, if the art typically engages in such experimentation. *See In re Certain Limited-Charge Cell Culture Microcarriers*, 221 U.S.P.Q. 1165, 1174, (Int'l Trade Comm'n 1983) *aff'd. sub nom., Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 U.S.P.Q. 428 (Fed. Cir. 1985).

In rejecting the claims, the Office impermissibly attempts to limit the invention to the scope of the examples. This is legally incorrect. As set forth in MPEP § 2164.02, "[f]or a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art (in view of level of skill, state of the art and the information in the specification) would expect the claimed genus could be used in that manner without undue experimentation." This is exactly what Applicants have provided. For example, Tables I - VIII and Examples 1-10 disclose data concerning methods for treating obesity by administering amylin or an amylin agonist to a human subject. Alone, this disclosure is sufficient such that one of ordinary skill in the art at the time the invention was made would have the ability to practice the invention commensurate in scope with the claims. Moreover, the terms "amylin" and "amylin agonist" are disclosed in the specification and have a well established meaning in the art. As described in the specification, the term "amylin" is understood to include compounds such as those defined in U.S. Pat. No. 5,234,906. Specification, for example, at page 13, line 1-22. The term "Amylin agonist" is also a term known in the art, and refers to a compound which mimics effects of amylin. Additionally, the specification provides numerous examples of amylin and amylin agonists capable of being used in the claimed methods without undue experimentation. Specification, for example, at page 15, line 1 - page 19, line 15.

Applicants disagree with the Office's assertion that the claimed invention should be limited to pramlintide. *Id.* at pages 16-21. Moreover, Applicants disagree with the Office's assertion that "[t]here is no showing however that administration of any amount of pramlintide, let alone any other non-pramlintide amylin agonist or amylin itself, administered 1 or 2 times a day did indeed induce obesity relief." *Id.* at page 19. Applicants respectfully submit that this is legally incorrect. There is no requirement to provide all of the ways that the claimed invention can be practiced. MPEP § 2164.01(b). The enablement requirement is satisfied as long as the

specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim. Applicants have satisfied this requirement by disclosing that pramlintide, when administered to a human, has the ability to treat obesity. As "amylin" and "amylin agonists" are disclosed in the instant specification and well known in the art, one of ordinary skill in the art at the time the invention was made would have the ability to practice the methods of treating obesity without undue experimentation in a manner that is commensurate in scope with the claims. Specification, for example, at page 13, lines 1-22 and page 15, line 1 - page 19, line 15.

The enablement requirement is met if the description enables any mode of making and using the claimed invention. *Engel Indus., Inc. v. Lockformer Co.,* 946 F.2d 1528, 1533. At a minimum, Applicants have satisfied this requirement by characterizing methods of treating obesity by administering pramlintide to humans. Specification, for example, at Examples 1-3 and Tables I - VII. Moreover, Applicants have disclosed numerous other amylin and amylin agonists capable of treating obesity. Specification, for example, at page 13, lines 1-22 and page 15, line 1 - page 19, line 15. Given at least this disclosure, one of ordinary skill in the art at the time the invention was made would have the ability to practice the claimed invention in a manner that is commensurate in scope with the claims without undue experimentation.

Applicants respectfully disagree with the Office's reliance on Baron *et al.* (*Current Drug Targets - Immune, Endocrine & Metabolic Disorders* 2(1): 63-82, 2002) and Ratner *et al.* (*Diabetes Technol. Ther.* 4:51-61, 2002) in rejecting the claims. Office Action at page 20. The Office asserts that both Baron *et al.* and Ratner *et al.* indicate the impracticability of using amylin as a therapeutic agent. *Id.* Applicants disagree. At the outset, Applicants note that the alleged "impracticability" of using native human amylin as a commercial drug product has no bearing on the enablement under 35 U.S.C. § 112. The Patent Office is not the FDA.

Moreover, contrary to the Office's position, Applicants assert that both Baron et al. and Ratner et al. actually support enablement of the claimed invention. That is, given the teachings of the instant specification coupled with the teachings of the prior art, one of ordinary in the art would have the ability to select amylin and amylin agonist peptides for use in the instant invention without undue experimentation. This further confirms that both amylin and amylin

agonists are well known compounds that have been widely characterized. Given this, one of ordinary skill in the art would have the requisite skill to practice the invention commensurate in scope with the claims without undue experimentation.

Applicants respectfully disagree with the Office's assertion that the obesity reducing effect of amylin or amylin agonists on an obese diabetic or non-diabetic human subject is unpredictable. *Id.* at page 21. Moreover, Applicants disagree with the Office's assertion that amylin and amylin agonists must be administered in conjunction with insulin in order to treat obesity. *Id.* at page 16-18 and 21. Post-filed experiments confirm the predictability of treating obesity in obese diabetic and non-diabetic humans, alike. For example, in Chapman *et al.* (*Diabetolgia* 48: 838-848, 2005), 11 men with type 2 diabetes and 15 non-diabetic obese men were treated for obesity by the administration of pramlintide. Compared with the placebo, pramlintide reduced the food intake of both the diabetic men and the non-diabetic obese men. Chapman *et al.* at abstract, Table 1, and Figure 1. This study indicates the effectiveness of amylin and amylin agonists in treating obesity in both diabetic men and non-diabetic obese men.

Applicants have demonstrated in Aronne *et al.* (*Am J Physiol Endocrinol Metab* 293: E620-E627, 2007) and Smith *et al.* (*The Journal of Clinical Endocrinology and Metabolism* 92(8):2977-2983, 2007) (enclosed in the IDS filed herewith) the effectiveness of amylin and amylin agonists on weight reduction and treatment. In Aronne *et al.*, 204 obese subjects were treated with the amylin analog pramlintide. Aronne *et al.* at page 2977. Pramlintide administration to obese subjects was well-tolerated and improved both weight and appetite control. *Id.* Similarly, in Smith *et al.*, 179 obese subjects were treated with pramlintide over a wide-range of doses. Smith *et al.* at Figures 2-6. In this study, pramlintide was successful in treating obesity as well as perceived control of eating. Smith *et al.* at abstract. Moreover, Smith *et al.* provides evidence that pramlintide can effectively treat obesity in a human subject without the co-administration of insulin.

Applicants disagree with the Office's assertion that one of skill in the art would not be able to treat obesity by administering amylin or amylin agonists to a human subject. *Id.* at page 16. The specification is replete with examples of functional variants, fragments, and derivatives of amylin and amylin agonists. Specification, for example, page 13, lines 1-22 and page 15, line

1 - page 19, line 15. For example, given at least SEQ ID NO: 12-17, one of ordinary skill in the art having read the specification would have the ability to make amino acid substitutions without undue experimentation. *Id.* Given this disclosure, one of ordinary skill in the art at the time the invention was made would also recognize which positions of amylin and amylin agonists are amenable to mutations and conservative substitutions. Moreover, to the extent that any additional experimentation may be required, Applicant notes that the performance of routine and well-known steps cannot create undue experimentation even if it is laborious. *See In re Wands*, 858 F.2d at 737, 8 U.S.P.Q.2d at 1404; *In re Angstadt,* 537 F.2d 498, 504, 190 U.S.P.Q. 214, 218-219 (C.C.P.A. 1976).

Given this disclosure, Applicants respectfully submit that one of ordinary skill in the art at the time the invention was made would have the ability to select variants, fragments, or derivatives of amylin and amylin agonists for practice with the claimed methods without undue experimentation. Applicants have sufficiently described the claimed invention such that one of skill in the art in light of the specification would be able to practice the invention commensurate in scope with the claims. Taken in combination, such disclosure provides adequate direction, including working examples, to teach the skilled artisan how to make and use the claimed invention without undue experimentation.

Accordingly, for at least these reasons, it is submitted that the claims are sufficiently enabled under 35 U.S.C. § 112, first paragraph, and withdrawal of this rejection is respectfully requested.

Rejections under 35 U.S.C. §112, second paragraph

The rejection of Claims 23, 24, 27, 29, 31-34, 37-39, 68, 72, 76, 80, 82, 84 and 95-97 under 35 U.S.C. § 112, second paragraph (Office Action, page 21, item 38) for alleged indefiniteness is respectfully traversed. Specific responses to the rejections follow:

(a) Claims 23, 33 and 76 as amended require that the amount administered is effective to treat obesity in the human subject, thereby obviating the alleged vagueness and indefiniteness asserted in the rejection.

(b) Claim 23 as amended requires a specified amount of the amylin or amylin agonist contemplated therein to be contained in the composition, thereby resolving the alleged indefiniteness and/or confusion asserted in the rejection.

(c) Claim 33 as amended requires a specified amount of the amylin or amylin agonist contemplated therein to be contained in the composition, thereby resolving the alleged indefiniteness and/or confusion asserted in the rejection.

(d) Applicants assume that reference to "Claim 43" (Office Action, page, 22, line 12) actually refers to "Claim 33" and have responded accordingly. Claims 23 and 33 as amended require specified amounts of an amylin or amylin agonist contemplated therein to be contained in the composition, thereby resolving the alleged indefiniteness and/or confusion asserted in the rejection.

(e) Applicants submit that Claims 24, 27, 29, 31, 32, 34, 37-39, 68, 72, 80, 82, 84 and 95-97 depend from base claims (i.e., 23, 33 or 76) which are not indefinite in view of the amendments provided herein.

Rejections under 35 U.S.C. §102

In order to anticipate a claim, a single prior art reference must provide each and every element set forth in the claim. In re Bond, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990). See also, MPEP §2131. The identical invention must be shown in complete detail as it is contained in the claim. Richardson v. Suzuki Motor Co., 9 USPQ2d 1913 (Fed. Cir. 1989).

Claims 23, 24, 27, 29, 31, 33, 34, 37-39, 80 and 82

The rejection of Claims 23, 24, 27, 29, 31, 33, 34, 37-39, 80 and 82 under 35 U.S.C. § 102(b) (Office Action, page 22, item 39) for alleged anticipation over Kolterman et al. (WO 96/40220 ("Kolterman '220") as evidenced by Tsanev (Id.), is respectfully traversed.

As noted above, the claimed invention is directed to methods of treating obesity in a human subject in need of such treatment through administration of a defined amount of an amylin or an amylin agonist. In contrast, as acknowleged by the Examiner (Office Action, page 23, lines 8-11), Kolterman '220 describes the use of an amylin agonist (i.e., pramlintide) for treating type II diabetes mellitus. However, Kolterman '220 does not teach the use of an amylin or an amylin agonist for treating obesity or demonstrate a reduction in body weight in those

patients administered an amylin or an amylin agonist. Indeed, Kolterman '220 is silent with regard to the effect of an amylin or an amylin agonist on body weight. Furthermore, Kolterman '220 is silent with respect to a target population in need of treatment for obesity.

In an attempt to cure the deficiency of Kolterman '220, the Examiner relies on Tsanev to provide alleged evidence that 80-90% of the diabetic patient population are obese (Office Action, page 23, lines 27-28). The Examiner asserts (Office Action, page 24, lines 1-6) that

> [g]iven Tsanev's express disclosure that 80 to 90% of type II diabetic patients are intrinically obese, and given Kolterman's ('220) express teaching that obesity is a characteristic of 'most patients with Type II diabetes mellitus', Kolterman's ('220) method of subcutaneous admiinistration of pramlintide to Type II diabetic patients in an amount that falls within the range recited in the instant claims necessarily serves as the claimed method of treating obesity and therefore anticipates the instantly claimed method.

Applicants disagree with the Examiner's assertion of anticipation by Kolterman '220 as evidenced by Tsanev. Anticipation based on inherency is appropriate only when the prior art relied upon necessarily includes all of the elements of the claims in question, Atofina v. Great Lakes Chemical Corp. (Id.), and is the natural result of following the instructions or examples of the prior art. See SmithKline Beecham Corp. v. Apotex Corp., (Id.); Schering Corp. v. Geneva Pharms., Inc., (Id.). The Court in Schering relied in part on the decision In re Cruciferous Sprouts Litigation, (Id.) wherein it was noted that to demonstrate inherency, it was necessary to show that the prior art necessarily, always functions in accordance with the claims addressed. The requirement that the teaching of a reference always, under any circumstances, necessarily satisfies the recitation of the claims to make out a case of inherent anticipation was reaffirmed by the Federal Circuit in Abbott Laboratories v. Baxter Pharmaceutical Products, Inc., (Id.). It is well settled that a determination of inherency cannot be established by probabilities or possibilities, but that it is incumbent upon the Examiner to establish the inevitability of the inherency which is propounded. In re Oelrich, (Id.); In re Wilding, (Id.)

Accordingly, a reference which teaches treating type II diabetic patients with an amylin or amylin agonist does not necessarily teach treating patient with obesity. Thus, the claimed invention cannot be recognized by one skilled in the art as inherently taught in the cited reference. Furthermore, the courts have held that the phrase "in need thereof" is meaningful, and that "the claims' recitation of a patient or a human 'in need' gives life and meaning to the

preambles' statement of purpose." Jansen v. Rexall Sundown, Inc. (Id.). Thus, Kolterman '220 cannot render unpatentable by inherency the subject population of the claimed invention. Accordingly, Kolterman '220 does not support anticipation of the claimed invention, and Applicants respectfully request reconsideration and withdrawal of the present rejection.

Claims 23, 24, 29, 33, 34 and 38

The rejection of Claims 23, 24, 29, 33, 34 and 38 under 35 U.S.C. §102(e)(2) (Office Action, page 25, item 40) for alleged anticipation over U.S. Patent No. 5,686,411 ('411 patent) as evidenced by Tsanev (Id.) is respectfully traversed.

As noted above, the claimed invention is directed to methods of treating obesity in a human subject in need of such treatment through administration of a defined amount of an amylin or an amylin agonist. In contrast, as acknowledged by the Examiner (Office Action, page 25, last paragraph continuing to page 26, line 2), the '411 patent discloses a method of treatment of diabetes mellitus in a mammal comprising the administration of a defined amylin agonist. However, nothing in the '411 patent teaches or suggests the use of an amylin or an amylin agonist in an amount effective to treat obesity, and nothing in the '411 patent teaches or suggests the identification of a subject in need of treatment for obesity.

In an attempt to cure the deficiency of the '411 patent, the Examiner relies on Tsanev to provide alleged evidence that 80-90% of diabetic patients are obese. Indeed, the Examiner acknowledges (Office Action, page 26, lines 13-15) that "[g]iven the art-known prevalence of intrinsic obesity in 80% to 90% of diabetic patients as disclosed by Tsanev (see abstract), at least 80-90% of the diabetic patients used in the method disclosed in the '411 patent qualify as human patients in need of treatment for obesity."

However, the law is clear that anticipation based on inherency is appropriate only when the prior art relied upon necessarily includes all of the elements of the claims in question, Atofina v. Great Lakes Chemical Corp. (Id.), and is the natural result of following the instructions or examples of the prior art. See SmithKline Beecham Corp. v. Apotex Corp., (Id.) In the present case, 80-90% falls short of the 100% (i.e., always, under any circumstanes) criterion required by the claims and required the law. Accordingly, the '411 patent does not anticipate the claimed

invention, and Applicants respectfully request reconsideration and withdrawal of the present rejection.

Claims 23, 24, 29, 31, 33, 34, 37-39, 80 and 82

The rejection of Claims 23, 24, 29, 31, 33, 34, 37-39, 80 and 82 under 35 U.S.C. §102(b) (Office Action, page 27, item 41) for alleged anticipation over Kolterman et al (Diabetologica 39: 492-499, 1996) ('Kolterman 1996') as evidenced by Itasaka et al. (Psychiatr. Clin. Neurosci. 54:340-341, 2000), is respectfully traversed.

As noted above, the claimed invention is directed to methods of treating obesity in a human subject in need of such treatment through administration of a defined amount of an amylin or an amylin agonist. In contrast, Kolterman 1996 describes the use of an amylin agonist, pramlintide, for treating patients with insulin-dependent diabetes mellitus and demonstrates that administration of the amylin agonist significantly reduces postprandial plasma glucose concentrations. However, Kolterman 1996 does not teach the use of the amylin agonist for treating obesity or demonstrate a reduction in body weight in those patients administered the amylin agonist. Furthermore, Kolterman 1996 is silent with regard to the effect of the amylin agonist on body weight. Kolterman 1996 does not report the weight of the subjects at the end of the study and nothing in the reference indicates that pramlintide had any effect on the weight of the subjects.

Furthermore, the Examiner asserts (Office Action, page 28, lines 27-28) that "the very active step recited in the instantly claimed method was disclosed and practice by Kolterman et al. in April, 1996." Applicants respectfully disagree with this assertion. The patient population of Kolterman 1996 is not necessarily the same as the claimed subject, i.e., a subject in need of a method of treating obesity. The Examiner has provided no extrinsic evidence to show that these patient populations are one in the same. Furthermore, Applicants respectfully note that the "fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic." In re Rijckaert, 9 F.3d 1531, 1534 (Fed. Cir. 1993); emphasis in original. "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the references, and that it would be so recognized by persons of ordinary skill. Inherency, however,

may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " In re Robertson 169 F.3d 743, 745 (Fed. Cir. 1999); emphasis added.

Specifically, the courts have held that the phrase "in need thereof" (e.g., as recited in independent Claims 1, 7, 14 and 16) is meaningful, and that "the claims' recitation of a patient or a human 'in need' gives life and meaning to the preambles' statement of purpose." Jansen v. Rexall Sundown, Inc. (Id.). Thus, Kolterman 1996 cannot render unpatentable by inherency the subject population of the claimed invention. Thus, Kolterman 1996 does not provide each and every element of the claimed invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of the present rejection.

Claims 23, 24, 27, 29, 33, 34, 37 and 38

The rejection of Claims 23, 24, 27, 29, 33, 34, 37 and 38 under 35 U.S.C. §102(e)(2) (Office Action, page 29, item 42) for alleged anticipation over U.S. Patent No. 5,321,008 ('008) as evidenced by Tsanev (Id.) is respectfully traversed.

As noted above, the claimed invention is directed to methods of treating obesity in a human subject in need of such treatment through administration of a defined amount of an amylin or an amylin agonist. In contrast, the '008 patent describes a method of treating diabetes mellitus in an insulin-requiring human who suffers from Type 1 or Type 2 diabetes mellitus. However, the '008 patent is silent with respect to obesity, treatment of obesity, or identification of a population in need of treatment for obesity. In an attempt to cure the deficiency in the '008 patent, the Examiner relies on Tsanev to provide alleged evidence that 80-90% of diabetic patients are obese. However, 80-90% falls short of the 100% (i.e., always, under any circumstanes) criterion required by the law as discussed in the response to Office Action item 38 above. See e.g., Schering Corp. v. Geneva Pharms., Inc., Id.; Abbott Laboratories v. Baxter Pharmaceutical Products, Inc., (Id.) Thus, the '008 patent does not provide each and every element of the claimed invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of the present rejection.

CONCLUSION

Applicants believe that all issues raised in the Office Action have been properly addressed in this response. Accordingly, reconsideration and allowance of the pending claims is respectfully requested. If the Examiner feels that a telephone interview would serve to facilitate resolution of any outstanding issues, the Examiner is encouraged to contact Applicants' representative at the telephone number below.

It is not believed that extensions of time or fees for net addition of claims are required beyond those that are otherwise provided for in the documents accompanying this paper. However, if any additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required thereof (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account Number 50-2387, referencing docket number 18528.230. Applicant(s) likewise authorize a charge to Deposit Account Number 50-2387 for any other fees related to the present application that are not otherwise provided for in the accompanying documents.

Respectfully submitted,

Date: October 23, 2007

/Milan M. Vinnola/
Milan M. Vinnola (Reg. No. 45,979)

ARNOLD & PORTER LLP
Attn: IP Docketing
555 Twelfth Street, NW
Washington, DC 20004-1206
202.942.5000 telephone
202.942.5999 facsimile